

REMARKS

Claims 101, 104-106, and 111-113, and 115-125 are pending in the present case. Applicants note with a appreciation that a number of prior rejections have been withdrawn. In the Office Communication mailed November 1, 2008, the Examiner made a number of new rejections. For clarity, these rejections are summarized below in the order in which they are addressed herein:

- I.** Claim 113 stands rejected under 35 U.S.C. §112, first paragraph as allegedly failing to comply with the written description requirement;
- II.** Claim 115 stands rejected under 35 U.S.C. §112, second paragraph as allegedly failing to particularly point out and distinctly claim the subject matter that applicants regard as the invention;
- III.** Claims 101, 104-106, 111-112, 115-117 and 123-125 stand rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Dahlberg;
- IV.** Claims 118-119 and 122 stand rejected under 35 U.S.C. 03(a) as allegedly being unpatentable over Dahlberg in view of Urdea;
- V.** Claims 120-121 stand rejected under 35 U.S.C. 03(a) as allegedly being unpatentable over Dahlberg in view of Corey;
- VI.** Claims 101-106 and 111-113, 115-120 and 122-125 stand provisionally rejected as being unpatentable under the judicially created doctrine of obviousness-type double patenting over co-pending Application Ser. No. 11/031,487, hereinafter "'487;";
- VII.** Claim 121 stands provisionally rejected as being unpatentable under the judicially created doctrine of obviousness-type double patenting over co-pending Application '487 in view of Corey;
- VIII.** Claims 101, 104-106 and 111-113, 115-120 and 122-125 stand provisionally rejected as being unpatentable under the judicially created doctrine of obviousness-type double patenting over co-pending Application Ser. No. 10/754,408, hereinafter "'408;" and
- IX.** Claim 121 stands provisionally rejected as being unpatentable under the judicially created doctrine of obviousness-type double patenting over co-pending Application '408 in view of Corey.

35 U.S.C. §112

I. Claim 113 stands rejected under 35 U.S.C. §112, first paragraph as allegedly failing to comply with the written description requirement. In particular, the Examiner asserts that the claim lacks support in the specification (Office Action page 3). For business reasons and without acquiescing to the Examiner's arguments, and reserving the right to prosecute the original or similar claims in one or more future applications, Applicants herein cancel Claim 13, rendering this rejection moot.

II. Claim 115 stands rejected under 35 U.S.C. §112, second paragraph as allegedly failing to particularly point out and distinctly claim the subject matter that applicants regard as the invention. In particular, the Examiner asserts that the term "second target" lacks proper antecedent basis (Office Action page 4). For business reasons and without acquiescing to the Examiner's arguments, and reserving the right to prosecute the original or similar claims in one or more future applications, Applicants herein cancel Claim 15, rendering this rejection moot.

35 U.S.C. §102

III. Claims 101, 104-106, 111-112, 115-117 and 123-125 stand rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Dahlberg. Applicants respectfully disagree.

Claim 101 recites a first oligonucleotide and a second oligonucleotide, each having a specific relationship to a target nucleic acid. The target nucleic acid comprises two regions that are contiguous to each other, with the second region being downstream of the first region; "downstream" refers to the 3' direction along a nucleic acid strand (see, *e.g.*, the specification at page 29, lines 11-13). The first oligonucleotide comprises a portion that is completely complementary to the first region of said target nucleic acid. The second oligonucleotide comprises several features: it comprises a 5' portion that is completely complementary to the second region of the target nucleic acid, and it additionally comprises a 3' portion. When aligned with the target nucleic acid according

to the various complementary portions, the first and second oligonucleotides can anneal to the target such that the contiguous first and second regions of the target are both completely annealed to form contiguous duplexes. When the nucleic acids are annealed in this fashion, the 3' portion of the second oligonucleotide overlaps with the duplex formed by the first oligonucleotide and the target nucleic acid (see, *e.g.*, Figure 32C).

The Examiner asserts that the claims do not require that the 5' portion be completely complementary to the entire, full length of the second region (Office Action page 4). To the extent that the 5' portion of the second oligonucleotide is completely complementary to less than the full length of said second region of the target nucleic acid, Applicants respectfully point out that the claims clearly state that the 5' portion is completely complementary to the region of said target nucleic acid that is downstream of and contiguous to said first region, and that this region to which the 5' portion of the second oligonucleotide is complementary is the "second region" of said target nucleic acid.

Nonetheless, for business reasons and without acquiescing to the Examiner's arguments, and reserving the right to prosecute the original or similar claims in one or more future applications, Applicants herein amend Claim 101 to recite that the 5' portion of the second oligonucleotide is completely complementary to the entire length of a second region of said target nucleic acid downstream of and contiguous to said first region.

Dahlberg fails to teach or suggest the use of a structure wherein first and second oligonucleotides are configured to anneal to contiguous regions of a target nucleic acid, wherein the second oligonucleotide further comprises a 3' portion. Comparing the structures of Dahlberg to the structures formed in the methods of the present invention, the duplex between the "substrate" strand and the "template" strand of Dahlberg (Figure 6, and 16E) can be compared to a duplex formed by between the target nucleic acid and the oligonucleotide of the present invention. The "primer" of Dahlberg can be compared to the second oligonucleotide. In the discussion of the primer, Dahlberg discusses primers that leave a gap between the 3' end of the primer and the downstream substrate duplex and discloses primers that leave no gap (see, *e.g.*, page 40, line 31 to page 41, line 2). However, even while teaching primers that leave no gap, such that the primer duplex

and the substrate duplex are contiguous, Dahlberg does not teach or suggest primers that additionally comprise a 3' portion that can overlap with the substrate duplex. Thus, Dahlberg does not teach or suggest the use of a primer or second oligonucleotide comprising a 3' portion such as is specified by the present claims. Dahlberg therefore fails to teach or suggest every element of Claims 101, 104-106, 111-112, 115-117 and 123-125 and does not anticipate these claims. As such, Applicants respectfully request that this rejection be removed.

35 U.S.C. §103

IV. Claims 118-119 and 122 stand rejected under 35 U.S.C. 03(a) as allegedly being unpatentable over Dahlberg in view of Urdea.

For the reasons recited above, Applicants submit that Dahlberg does not teach or suggest oligonucleotides that that can form an overlap structure, as described above. Urdea fails to overcome this deficiency. Urdea teaches the cleavage of a labeled oligonucleotide on a solid support using, *e.g.*, a restriction enzyme. Urdea does not teach the recited combination of: 1) first and a second oligonucleotides that comprise defined regions of complementarity to a target nucleic acid such that they form an overlapped structure when annealed to the target nucleic acid; and 2) a thermostable 5' nuclease that lacks synthetic activity and that functions to cleave a nucleic acid cleavage structure at a temperature of at least 55°C, nor does Urdea teach the cleavage of such overlapping structures with a thermostable 5' nuclease that lacks synthetic activity and that functions to cleave a nucleic acid cleavage structure at a temperature of at least 55°C. While Applicants do not acquiesce that the other elements necessary for establishing *prima facie* obviousness have been met, Applicants submit that the combination of Dahlberg and Urdea does not teach or suggest all the limitations of Claims 105-106, 118-119 and 122, and cited art therefore fails to establish *prima facie* obviousness. Applicants respectfully request that this rejection be removed.

V. Claims 120-121 stand rejected under 35 U.S.C. 03(a) as allegedly being unpatentable over Dahlberg in view of Corey.

For the reasons recited above, Applicants submit that Dahlberg does not teach or suggest oligonucleotides that that can form an overlap structure, as described above. Corey fails to overcome this deficiency. Corey teaches the attachment of a polypeptide to a nucleic acid to enhance hybridization. Corey does not teach the recited combination of: 1) first and a second oligonucleotides that comprise defined regions of complementarity to a target nucleic acid such that they form an overlapped structure when annealed to the target nucleic acid; and 2) a thermostable 5' nuclease that lacks synthetic activity and that functions to cleave a nucleic acid cleavage structure at a temperature of at least 55°C, nor does Corey teach the cleavage of such overlapping structures with a thermostable 5' nuclease that lacks synthetic activity and that functions to cleave a nucleic acid cleavage structure at a temperature of at least 55°C. While Applicants do not acquiesce that the other elements necessary for establishing prima facie obviousness have been met, Applicants submit that the combination of Dahlberg and Corey does not teach or suggest all the limitations of Claims 120 and 121, and cited art therefore fails to establish prima facie obviousness. Applicants respectfully request that this rejection be removed.

Obviousness-type Double Patenting

VI. - IX Claims 101-106 and 111-113, 115-120 and 122-125 stand provisionally rejected as being unpatentable under the judicially created doctrine of obviousness-type double patenting over co-pending Application Ser. No. 11/031,487, hereinafter "'487;" Claim 121 stands provisionally rejected as being unpatentable under the judicially created doctrine of obviousness-type double patenting over co-pending Application '487 in view of Corey; Claims 101, 104-106 and 111-113, 115-120 and 122-125 stand provisionally rejected as being unpatentable under the judicially created doctrine of obviousness-type double patenting over co-pending Application Ser. No. 10/754,408, hereinafter "'408;" and Claim 121 stands provisionally rejected as being unpatentable under the judicially created doctrine of obviousness-type double patenting over co-pending Application '408 in view of Corey.

The two applications cited by the Examiner in making the above-recited obviousness-type double patenting rejections, co-pending Application Ser. No.

10/754,408, filed 01/09/2004 and co-pending Application Ser. No. 11/031,487, filed 01/07/2005, are both substantially later filed than the instant application (which was filed 02/12/2002, and which claims priority to yet earlier filed cases). In accordance with the MPEP § 804 I.B.1 procedure regarding provisional double patenting rejections involving earlier and later filed applications, Applicants respectfully request that this double patenting rejection be held in abeyance until such time as a claim is found to be allowable, and that each of these double patenting rejections then be withdrawn from this earlier filed case.

CONCLUSION

For the reasons set forth above, it is respectfully submitted that all grounds for rejection have been addressed and Applicant's claims should be passed to allowance. Should the Examiner believe that a telephone interview would aid in the prosecution of this application, Applicants encourages the Examiner to call the undersigned collect at (608) 218-6900.

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